

Claims

5. Recombinant CELO virus or CELO virus DNA, characterized in that it carries a modification of the wild type CELO DNA that results in a complete loss of Gaml expression or an inhibition of functional Gaml expression.

10. The recombinant CELO virus or CELO virus DNA of claim 1, characterized in that the region spanning nt 37391-38239 of the CELO wild type virus genome is completely or partially deleted or altered or contains an insertion.

15. The recombinant CELO virus or CELO virus DNA of claim 2, characterized in that the region spanning nt 36818-37972 of the wild type CELO virus genome is deleted.

20. The recombinant CELO virus or CELO virus DNA of claim 1, characterized in that it contains a modification in the Gaml transcriptional control sequences.

25. The recombinant CELO virus or CELO virus DNA of claim 1, characterized in that it further contains a deletion of or within a region selected from the regions spanning nt 41731-43684, nt 41523-43684, nt 41002-43684 and nt 40065-43684.

30. The recombinant CELO virus or CELO virus DNA of claim 1, characterized in that it further contains a deletion spanning nt 794-1330.

Sub C3

7. The recombinant CELO virus DNA of claim 1 contained on a plasmid that can be replicated in prokaryotic or eucaryotic cells.

5 8. The recombinant CELO virus or CELO virus DNA of claim 1, characterized in that it contains a foreign DNA insertion in place of one or more deletions.

9. The recombinant CELO virus or CELO virus DNA of claim 8 characterized in that the foreign DNA encodes an antigen derived from an animal pathogen.

10 10. The recombinant CELO virus or CELO virus DNA of claim 9 characterized in that the pathogen is avian.

11. The recombinant CELO virus or CELO virus DNA of claim 8 characterized in that the foreign DNA encodes a human protein.

15 12. The recombinant CELO virus or CELO virus DNA of claim 11, characterized in that the DNA encodes a therapeutically active protein.

Sub C4

20 13. The recombinant CELO virus or CELO virus DNA of claim 12, characterized in the DNA encodes an immunostimulatory protein.

14. The recombinant CELO virus or CELO virus DNA of claim 13, characterized in that the immunostimulatory protein is a cytokine.

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Sub C5

15. The recombinant CELO virus or CELO virus DNA of claim 11, characterized in that the foreign DNA encodes a tumor antigen or a fragment thereof.

5 16. The recombinant CELO virus or CELO virus DNA of claim 11, characterized in that the foreign DNA encodes an antigen derived from a human pathogen.

10 17. A method for producing the recombinant CELO virus of claim 1, characterized in that the modification of CELO virus DNA is carried out on plasmid-borne CELO virus DNA and that the recombinant CELO virus DNA is introduced into a host that supports virus replication and the host is incubated under conditions that allow amplification of the virus.

15 18. A method of claim 17 characterized by the following steps

20 a) carrying out the DNA modification on plasmid-borne CELO virus DNA,

b) introducing the recombinant CELO virus DNA into a host cell that supports virus replication, said host cell being a primary cell or a cell from an immortalized cell line,

c) exposing the cells to a heat shock treatment before, simultaneously with or after step b),

d) growing the cells for a period of time sufficient to obtain the desired number of viruses.

25 19. The method of claim 18, characterized in that the heat shock treatment comprises exposing the cells to temperatures above 43°C for period of time sufficient to complement the replication defect.

20. The method of claim 19, characterized in that the cells are exposed to 45°C.
21. The method of claim 19, characterized in that cells are exposed to the heat shock treatment for 30 - 5 120 minutes.
22. The method of claim 21, characterized in that cells are exposed to the heat shock treatment for 90 minutes.
23. The method of claim 17 characterized in that the 10 host is an avian embryo which is infected with more than 10^7 virus particles per embryo.
24. A method for producing the recombinant CELO virus of claim 1 characterized by the following steps 15 a) carrying out the DNA modification on plasmid-borne CELO virus DNA,
b) introducing the recombinant CELO virus DNA into a host cell that supports virus replication, said host cell being a primary cell or a cell from an immortalized cell line,
c) exposing the cells to a heat shock treatment before, simultaneously with or after step b),
d) growing the cells for a period of time sufficient to obtain the desired number of viruses,
e) introducing the viruses obtained in d) into an 20 avian embryo at a number higher than 10^7 virus particles per embryo and incubating the embryo for a period of time sufficient to amplify the virus.
25. The method of claim 23, characterized in that the embryo is chicken.

26. The method of claim 17, wherein the host cell carries a DNA from which hsp40 or another protein upregulated by Gaml is expressed.

27. The method of claim 26, wherein the host cell 5 carries a plasmid encoding hsp40 or another protein upregulated by Gaml.

28. The method of claim 26, wherein the host cell is 10 coinfected with a recombinant adenovirus directing the synthesis of hsp40 or another protein upregulated by Gaml.

29. The method of claim 26, wherein the host cell is infected with a CELO virus into whose genome an expression cassette encoding hsp40 or another protein upregulated by Gaml has been inserted.

30. A vaccine against an infectious disease of an animal comprising CELO virus of claim 9.

31. A vaccine against an infectious disease of a bird comprising CELO virus of claim 10.

32. A vaccine against an infectious disease of a human comprising CELO virus of claim 16.

33. A pharmaceutical composition containing as an active ingredient a CELO virus of claim 12.

34. The CELO virus of claim 12 for the manufacture of a tumor vaccine.

25 35. Method for producing a recombinant protein of interest, characterized in that the recombinant

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CELO virus of claim 8, wherein the foreign DNA encodes the protein of interest, is introduced into avian embryos at a number higher than 10^7 particles per embryo and the virus is allowed to amplify to produce the protein of interest and the protein is recovered.

5 36. The method of claim 35, wherein DNA encoding the protein of interest is fused to a DNA molecule encoding an immunoglobulin Fc domain.

10 37. The method of claim 36, wherein the foreign DNA further comprises a signal sequence.

38. The method of claim 37, wherein the protein of interest is a secreted protein and the signal sequence is its natural signal sequence.

15 39. The method of claim 38, wherein the signal sequence is derived from a protein naturally secreted into chicken eggs, said protein being different from the protein of interest.

20 40. The method of claim 39, wherein the signal sequence is derived from ovalbumin, avidin, conalbumin or lysozyme.

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